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| Attorney Docket Number | 20052YP |
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| Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | COMPLETE IF KNOWN | | |
|  | | | Application Number | 09/601,582 | |
| | | | Filing Date | December 4, 2000 | |
| | | | First Named Inventor | Liu, et al. | |
| | | | Group Art Unit | 1646 | |
| | | | Examiner Name | Kaufman | |
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| NON PATENT LITERATURE DOCUMENTS | | |
|---------------------------------|----------|--|
| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication. |
| <i>CMH</i> | | Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Research, Vol. 25, No. 17, 1997. |
| <i>/</i> | | Amatruda, et al., "Specific Interactions of Chemoattractant Factor Receptors with G-proteins*", The Journal of Biological Chemistry, Vol. 268, No. 14, pp. 10139-10144, May 15, 1993. |
| <i>/</i> | | Andrade, et al., "A G Protein Couples Serotonin and GABAB Receptors to the Same Channels in Hippocampus", Vol. 234, pp. 1261-1265, 1986. |
| <i>/</i> | | Blakely, et al., "Vaccinia-T7 Polymerase Expression System: Evaluation for the Expression Cloning of Plasma Membrane Transporters", Analytical Biochemistry, Vol. 194, pp. 302-308, 1991. |
| <i>/</i> | | Bormann & Feigenspan, "GABAC Receptors", Trends Neurosci., Vol. 18, pp. 515-518, 1995. |
| <i>/</i> | | Bowery, et al., "GABAB receptors and their significance in mammalian pharmacology", Trends in Pharmacological Sciences, Vol. 10, No. 10, pp. 401-407, 1989. |
| <i>/</i> | | Bowery & Pratt, "GABAB Receptors as Targets for Drug Action", Arzneim.-Forsch/Drug Res., Vol. 42, pp. 215-223, 1992. |
| <i>/</i> | | Bradley, et al., "Spacial and Temporal Expression of alpha- and beta-Thyroid Hormone Receptor mRNAs, Including the beta-2-Subtype, in the Developing Mammalian Nervous System", J. of Neurosci., Vol. 12, pp. 2288-2302, 1992. |
| <i>/</i> | | Brakeman, et al., "Homer: a protein that selectively binds metabotropic glutamate receptors", Nature, Vol. 386, pp. 284-288, 1997. |
| <i>/</i> | | Brooker, et al., "Advances in Cyclic Nucleotide Research", Adv. Cyclic Nucleic Research, Vol. 10, pp. 1-33, 1979. |
| <i>/</i> | | Chou & Heinrikson, "Prediction of the Tertiary Structure of the Complement Control Protein Module", Journal of Protein Chemistry, Vol. 16, pp. 765-773, 1997. |
| <i>/</i> | | Clark, et al., "Multiple Regions of Ligand Discrimination Revealed by Analysis of Chimeric Parathyroid Hormone 2 (PTH2) and PTH/PTH-Related Peptide (PTHrP) Receptors", Molecular Endocrinology, Vol. 12, pp. 193-206, 1998. |
| <i>/</i> | | Couve, et al., "Intracellular Retention of Recombinant GABAB Receptors", J. Biol. Chem., Vol. 273, pp. 26361-26367, 1998. |
| <i>/</i> | | Cunningham & Wells, "High-Resolution Epitope Mapping of hGH-Receptor Interactions by Alanine Scanning Mutagenesis", Science, Vol. 244, pp. 1081-1085 (1989). |
| <i>/</i> | | Gahwiler, et al., "GABAB-receptor-activated K ⁺ current in voltage-clamped CA3 pyramidal cells in hippocampal cultures", Proc. Natl. Acad. Sci., Vol. 82, pp. 1558-1562, 1985. |

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| Examiner Signature | <i>Clara M. Kauf</i> | Date Considered | 6/21/04 |
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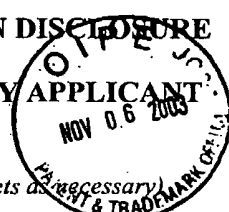
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| NON PATENT LITERATURE DOCUMENTS | | |
|---------------------------------|----------|--|
| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication. |
| CHT | | Gonzalez & Tsien, "Voltage Sensing by Fluorescence Resonance Energy Transfer in Single Cells", Biophysical Journal, Vol. 69, pp. 1272-1280, 1995. |
| / | | Gonzalez & Tsien, "Improved indicators of cell membrane potential that use fluorescence resonance energy transfer", Chemistry & Biology, Vol. 4, pp. 269-277, 1997. |
| / | | Graminski, et al., "Pigment Dispersion in Frog Melanophores Can Be Induced by a Phorbol Ester or Stimulation of a Recombinant Receptor That Activates Phospholipase C", J. Biol. Chem., Vol. 268, pp. 5957-5967, 1993. |
| / | | Guan, et al., "Enhancement of Membrane Insertion and Function in a Type IIIb Membrane Protein following Introduction of a Cleavable Signal Peptide", J. Biol. Chem., Vol. 267, pp. 21995-21998, 1992. |
| / | | Hebert, et al., "A Peptide Derived from a β 2-Adrenergic Receptor Transmembrane Domain Inhibits Both Receptor Dimerization and Activation", J. Biol. Chem., Vol. 271, pp. 16384-16392, 1996. |
| / | | Hess, et al., "Cloning and Pharmacological Characterization of a Human Bradykinin (BK-2) Receptor", Biochem. and Biophys. Res. Comm., Vol. 184, No. 1, pp. 260-268, 1992. |
| / | | Hodgson, "Receptor Screening and the Search for New Pharmaceuticals", Bio/Technology, Vol. 10, pp. 973-980, 1992. |
| / | | Hopp & Woods, "Prediction of protein antigenic determinants from amino acid sequences", Proc. Natl. Acad. Sci. USA, Vol. 78, No. 6, pp. 3824-2828, June 1981. |
| / | | Howard, et al., "A Receptor in Pituitary and Hypothalamus That Functions in Growth Hormone Release", Science, Vol. 273, pp. 974-977, 1996. |
| / | | Jameson, et al., "The antigenic index: a novel algorithm for predicting antigenic determinants", BABIOS, Vol. 4, No. 1, pp. 181-186, 1988. |
| / | | Kohler & Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity", Nature, Vol. 256, pp. 495-497, 1975. |
| / | | Kolakowski, et al., "ProSearch: Fast Searching of Protein Sequences with Regular Expression Patterns Related to Protein Structure and Function", BioTechniques, Vol. 13, No. 6, pp. 919-921, 1992. |
| / | | Lerner, "Tools for investigating functional interactions between ligands and G-protein-coupled receptors", Trends Neurosci., Vol. 17, pp. 142-146, 1994. |
| / | | Lofts, et al., "Specific short transmembrane sequences can inhibit transformation by the mutant neu growth factor receptor in vitro and in vivo", Oncogene, Vol. 8, pp. 2813-2820, 1993. |
| CHT | | Maidment, et al., "Microdialysis of Extracellular Endogenous Opioid Peptides From Rat Brain In Vivo", Neuroscience, Vol. 33, No. 3, pp. 549-557, 1989. |

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| Examiner Signature | <i>Chau M. King</i> | Date Considered | 6/21/04 |
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| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication. |
| <i>CKM</i> | | McKee, et al., "Molecular Analysis of Rat Pituitary and Hypothalamic Growth Hormone Secretagogue Receptors", Molecular Endocrinology, Vol. 11, pp. 415-423, 1997. |
| <i>/</i> | | McKernan & Whiting, "Which GABAA-receptor subtypes really occur in the brain?", Trends Neurosci., Vol. 16, pp. 139-143, 1996. |
| <i>/</i> | | Misgeld, et al., "A Physiological Role for GABAB Receptors and the Effects of Baclofen in the Mammalian Central Nervous System", Vol. 46, pp. 423-462, 1995. |
| <i>/</i> | | Ng, et al., "Dopamine D2 Receptor Dimers and Receptor-Blocking Peptides", Biochemical and Biophysical Research Communications, Vol. 227, pp. 200-204, 1996. |
| <i>/</i> | | Nicholson, et al., "The gene for hereditary sensory neuropathy type 1 (HSN-1) maps to chromosome 9q22.1-122.3", Nature Genetics, Vol. 12, pp. 101-104, 1996. |
| <i>/</i> | | North, ^{Drug receptors and the inhibition of nerve cells} "Twelfth Gaddum Memorial Lecture" , Br. J. Pharmacol., Vol. 98, pp. 13-28, 1989. |
| <i>/</i> | | Buhl, et al., "Selective coupling of the human anaphylatoxin C5a receptor and alpha 16 in human kidney 293 cells", FEBS Lett., Vol. 323, No. 1, 2, pp. 132-132, 1993. |
| <i>/</i> | | Offermanns, et al., "Galpha15 and Galpha16 Couple a Wide Variety of Receptors to Phospholipase C", J. Biol. Chem., Vol. 270, No. 28, pp. 15175-15180, 1995. |
| <i>/</i> | | O'Hara, et al., "The Ligand-Binding Domain in Metabotropic Glutamate Receptors Is Related to Bacterial Periplasmic Binding Proteins", Neuron, Vol. 11, pp. 41-52, 1993. |
| <i>/</i> | | Pearson, et al., "Comparison of DNA Sequences with Protein Sequences", Genomics, Vol. 46, pp. 24-36, 1997. |
| <i>/</i> | | Perkins, et al., "A Study of the Structure of Human Complement Component Factor H by Fourier Transform Infrared Spectroscopy and Secondary Structure Averaging Methods", Vol. 27, pp. 4004-4012, 1988. |
| <i>/</i> | | Pin and Duvoisin, "Review: Neurotransmitter Receptors I The Metabotropic Glutamate Receptors: Structure and Functions", Neuropharmacology, Vol. 14, No. 1, pp. 1-23, 1995. |
| <i>/</i> | | Potenza & Lerner, "A Rapid Quantitative Bioassay for Evaluating the Effects of Ligands Upon Receptors That Modulate cAMP Levels in a Melanophore Cell Line", Pigment Cell Research, Vol. 5, pp. 372-375, 1992. |
| <i>/</i> | | Potenza, et al., "A Method for Evaluating the Effects of Ligands upon G3 Protein-Coupled Receptors Using a Recombinant Melanophore-Based Bioassay", Analytical Biochemistry, Vol. 206, pp. 315-322, 1992. |
| <i>CKM</i> | | Romano, et al., "Metabotropic Glutamate Receptor 5 Is A Disulfide-linked Dimer", J. Biol. Chem., Vol. 271, No. 45, pp. 28612-28616, 1996. |

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| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication. |
| CK | | Rutter, et al., "Real-time imaging of gene expression in single living cells", Chemistry & Biology, Vol. 5, pp. R285-R290, 1998. |
| + | | Sequier, et al., "Mapping of brain areas containing RNA homologous to cDNAs encoding the alpha and beta subunits of the rat GABAA gamma-aminobutyrate receptor", Proc. Natl. Acad. Sci. USA, Vol. 85, pp. 7815-7819, October 1988. |
| + | | Watson, et al., "The Fine Structure of Bacterial and Phage Genes", Molecular Biology of the Gene", Fourth Edition, The Benjamin/Cummings Press, pp. 214-238, 1987. |
| + | | White, et al., "Heterodimerization is required for the formation of a functional GABAB receptor", Nature, Vol. 396, pp. 679-682, 1998. |
| + | | Yokomizo, et al., "A G-protein-coupled receptor for leukotriene B4 that mediates chemotaxis", Nature, Vol. 387, pp. 620-624, 1997. |
| + | | Zlokarnik, et al., "Quantitation of Transcription and Clonal Selection of Single Living Cells with Beta-Lactamase as Reporter", Science, Vol. 279, pp. 87-88, 1988. |
| CK | | GenBank Accession No. Y10369 19 Dec. 2002. |
| + | | GenBank Accession No. Y11044 08 Oct. 1998. |
| + | | GenBank Accession No. T10370 27 Jul. 1993. |
| + | | GenBank Accession No. AJ012188 24 Apr. 1999. |
| + | | GenBank Accession No. 3776096 24 Apr. 1999. |
| + | | GenBank Accession No. AF074483 07 Jan. 1999. |
| + | | GenBank Accession No. AF056085, 10 Apr. 2000. |
| CK | | GenBank Accession No. AJ012185, 24 Apr. 1999. |
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Kaupmann, et al., "Expression cloning of GABA_B receptors uncovers similarity to metabotropic glutamate receptors", *Nature*, Vol. 386, pp. 239-246, 1997

Kaupmann, et al., "GABAB-receptor subtypes assemble into functional heteromeric complexes", *Nature*, Vol. 396, pp.683-687, 1998.

Jones, et al., "GABAB receptors function as a heteromeric assembly if the subunits GABABR1 and GABABR2", *Nature*, Vol. 396, pp. 674-678, 1998.

Kuner, et al., "Role of Heteromer Formation in GABAB Receptor Function", *Science*, Vol. 283, pp. 74-77, 1999.

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